Remarks

Amendments

The specification has been amended to correct an obvious error. The amendment adds no new matter and Applicants respectfully request its entry.

Claims 1, 18, and 19 are amended to recite methods of isolating a clone comprising a polynucleotide, vaccine target or diagnostic target. Support for the amendment can be found in the specification at, *inter alia,* page 14, lines 1-6. These are not narrowing amendments. New claims 20-26 are added herein. Support for claims 20-22 can be found in the specification at, *inter alia*, page 11, lines 22-23. Support for claims 23-25 can be found in the specification at, *inter alia*, page 7, lines 9-22. Support for claims 26-28 can be found in the specification at, *inter alia*, page 11, line 19.

Amendments to the claims are made without prejudice or disclaimer. They are fully supported by the specification as filed and do not introduce new matter. Additionally, these amendments are not and should not be construed as admissions regarding the patentability of the claimed or canceled subject matter. Applicants reserve the right to pursue the subject matter of previously presented claims or any broader claims in this or in any other appropriate patent application. Accordingly, Applicants respectfully request the entry of the amendments presented.

Interview Summary

On November 12, 2010, the undersigned, Examiner Steele, and Examiner Hama participated in a telephonic interview. Applicants thank the Examiners for their time and comments. No exhibits were shown and no demonstrations were conducted. All pending claims were discussed. The art cited in the Office Action of July 26, 2010, was discussed. Amendments to the claims as presented herein were discussed. The principal arguments of the applicant were as presented in the response filed on October 26, 2010. No other pertinent matters were discussed. Examiner Steele agreed to consider a supplemental amendment.

Objection to Claim 7

The Applicants understand that the objection to claim 7 will be withdrawn in view of the Examiner Interview.

Rejection of Claims 1-5, 7-10, 18 and 19 Under 35 U.S.C. § 101

The Applicants understand that this rejection will be withdrawn.

Rejection of Claims 1-5, 7-10, 18 and 19 Under 35 U.S.C. § 112, first paragraph

The Applicants understand that this rejection will be withdrawn.

Rejection of Claims 18 and 19 Under 35 U.S.C. § 112, first paragraph

Claims 18-19 stand as rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Applicants respectfully traverse the rejection and request that the arguments presented in the Response of October 26, 2010, be considered along with the additional comments presented herein.

During the Examiner interview Examiner Steele asserted that the Declaration of Dr. Handfield was not commensurate in scope with the scope of the claims because the claims relate to the screening methods for certain polynucleotides from any microbe or pathogen while the Declaration related to screening methods for certain polynucleotides from less than all microbes and pathogens.

The MPEP states that Applicants may file:

> a declaration after the filing date which demonstrates that the claimed invention works. However, the examiner should carefully compare the steps, materials, and conditions used in the experiments of the declaration with those disclosed in the application to make sure that they are commensurate in scope; i.e., that the experiments used the guidance in the specification as filed and what was well known to one of skill in the art. Such a showing also must be commensurate with the scope of the claimed invention, i.e., must bear a reasonable correlation to the scope of the claimed invention.

See MPEP 2164.05. Applicants assert that the demonstration that the methods of the invention were used to identify clones comprising polynucleotides expressed only *in vivo* in a number of different microbes are commensurate in

scope with the claims when considered both individually and combined as a whole.

The steps, materials, and conditions used in the experiments of the declaration are commensurate in scope with those disclosed in the application; *i.e.*, that the experiments used the guidance in the specification as filed and what was well known to one of skill in the art. For example, both Handfield *et al.* (Trends Microbiol. 8:336 (2000) (of record)) and Rollins *et al.* (Cell. Microbiol. 7:1 (2005) (copy attached)) describe the IVIAT methods of the invention. *See e.g.*, Specification, Figure 1; Handfield Figure 1; Rollins Figure 1. The Declaration of Dr. Handfield submitted on October 26, 2010, states that "[t]he specification of the instant application terms the methods of the invention as 'IVIAT methodology." *See* specification page 10, lines 10-15. The term 'IVIAT methodology' has also been recognized in the art as the name of methods as described in the instant invention." *See* Declaration, ¶ 2.

The following papers describe the identification of clones comprising a polynucleotide, diagnostic target and/or vaccine target of a microbe or pathogen that is expressed only *in vivo* using the IVIAT techniques as described in the instant specification:

Using the methodology of Handfield, Dantas *et al.* (Microbes Infect., 11:895 (2009) (copy attached)) teaches that "[w]ith the purpose of identifying antigenic proteins potentially expressed during the fungal infection process, here we applied the *in vivo*-induced antigen technology (IVIAT)." *See* page 896, left col.

Citing the methodology of Handfield, Kumar *et al.* (Microbial. Pathogenesis, 2010 (copy attached)) teaches that "we used IVIAT to identify *M. tuberculosis* genes exclusively induced during human infection . . . ." *See* page 2, left col.

Citing the methodology of Handfield, Rollins *et al.*, (PLoS ONE, 3:1824 (2008) (copy attached)) teaches that "[w]e applied IVIAT to *Bacillus anthracis* and identified [many] proteins." *See* abstract.

Citing the methodology of Rollins, Harris *et al.* (Infect. Immun. 74:5161 (2006) (copy attached)) teaches that "we applied an immunological screening technique termed *in vivo*-induced antigen technology (IVIAT) [to identify serovar Typhi proteins]. *See* page 5162, left col.

Citing the methodology of Handfield, Salim *et al.* (Infect. Immun. 73:6026 (2005) (copy attached)) teaches that we "investigate[d] the pathogenesis of invasive [Group A *Streptococcus*] infections by using IVIAT." *See* page 6026, right col.

Citing the methodology of Handfield, John *et al.*, (Infect. Immun. 73:2665 (2005) (copy attached)) teaches that "we used a modified immuno-screeing technique called *in vivo*-induced antigen technology (IVIAT), which enables identification of antigens expressed specifically during infection but not during growth in standard laboratory media." *See* page 2666, left col.

Citing the methodology of Handfield, Kim *et al.*, (Infect. Immun. 71:5461 (2003) (copy attached)) teaches that "we used *in vivo*-induced antigen technology (IVIAT), a novel method designed to screen microbial genes expressed specifically during human infections, to identify *V. vulnificus* genes expressed preferentially *in vivo*." *See* page 5462, left col.

Citing the methodology of Handfield, Hang *et al.* (PNAS, 100:8508 (2003) (copy attached)) teaches that "[t]he aim of this study was to use IVIAT to identify *V. cholerae* genes specifically expressed during human infection." *See* page 8509, left col.

Citing the methodology of Handfield, Deb *et al.* (Tuberculosis, 82:175 (2002) (copy attached)) teaches "[i]n this study, using the IVIAT approach, we have identified six new ORFs of *M. tuberculosis* as potential therapeutic targets." *See* page 176, left col.

Citing the methodology of Handfield, Cao *et al.* (FEMS Microbio. Lett., 237:97 (2004) (copy attached)) teaches that "[t]he purpose of the present paper is to report the identity and further characterize the first nine of 116 [*Actinobacillus actinomycetemcomitans*] antigens that were found with IVIAT." *See* page 98, left col.

Citing the methodology of Handfield, Song *et al.* (Ann. Peridontol., 7:38 (2002) (copy attached)) teaches that "IVIAT has proven useful in identifying previously unknown *in vivo*-induced [*A. actinomycetemocomitans* and *P. gingivalis*] genes that are likely involved in virulence and are thus excellent candidates for use in diagnostic and therapeutic strategies, including vaccine design." *See* abstract, page 38.

Citing the methodology of Handfield, Yoo *et al.* (FEMS Microbiol. Lett., 275:344 (2007) (copy attached)) teaches that "[i]n this study, *in vivo* induced antigen technology (IVIAT) was applied in order to identify protein antigens that are specifically expressed during an infection of *T. forsythia* in patients with periodontal disease." *See* page 345, left col.

Citing the methodology of Handfield, Yong *et al.* (Sci. China Ser. C-Life Sci., 52:942 (2009) (copy attached)) teaches that "[i]n the present study, we utilized *in vivo* induced antigen technology (IVIAT), an immunogenic technique, to identify serovar Typhi antigens expressed during infection." *See* page 943, left col.

Citing the methodology of Handfield, Lowry *et al.* (Vet. Microbiol., 142:367 (2010) (copy attached)) teaches that "we have used the [IVIAT] methodology to identify bacterial antigens relevant to the survival of *B. abortus* in elk, with the anticipated outcome of gaining a better understanding of what virulence effectors are important in this host-pathogen system, as well as to potentially identify new diagnostic targets and/or sub-unit vaccine candidates that may be applied to several different susceptible hosts." *See* page 368, left col.

Each of these references uses steps, materials, and conditions as disclosed in the instant specification and are therefore commensurate in scope with the specification. Applicants note that there is more than one way to demonstrate the universality of the generic methods of the invention. For example, enablement for a generic claim can be demonstrated by (1) a single example or piece of evidence that shows the methods can be used to screen all microbes or pathogens; or (2) by several pieces of evidence or examples that demonstrate the methods can be used to screen different microbes or pathogens

in single instances. In this case, the Applicants have provided evidence that the claimed methods can indeed be used to screen a multitude of microbes herein and in the Declaration of Dr. Handfield submitted on October 26, 2010. "A declaration or affidavit is, itself, evidence that must be considered." MPEP § 2164.05 (emphasis in the original). "The evidence provided by the applicant need not be conclusive but merely convincing to one skilled in the art." MPEP § 2164.05. Applicants have provided extensive evidence that the claimed methods are enabled by providing evidence that those of ordinary skill in the art have successfully used the methods of the invention as described in the specification to identify clones comprising polynucleotides, diagnostic targets, and vaccine targets that are expressed only *in vivo*.

Furthermore, under 35 U.S.C. § 112, all that is required for enablement is that the specification describe the invention in such terms as to enable a person skilled in the art to make and use the invention. The test of enablement is whether one reasonably skilled in the art (1) could make and use the invention (2) from the disclosures in the patent coupled with information known in the art (3) without undue experimentation. *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988); *United States v. Telectronics, Inc.*, 857 F.2d 778 (Fed. Cir. 1988); M.P.E.P. § 2164.01. Applicants submit that it is a matter of routine experimentation to use the methods of the invention to isolate clones comprising polynucleotides, vaccine targets, and diagnostic targets. The law clearly states that "a considerable amount of experimentation is permissible, if it is merely routine." *In re Wands,* 858 F.3d 731, 737 (Fed. Cir. 1988). Furthermore, the fact that experimentation may be complex does not necessarily make it undue. *Massachusetts Institute of Technology v. A.B. Fortia,* 774 F.2d 1104 (Fed. Cir. 1985); *In re Wands,* 858 F.2d at 737 (Fed. Cir. 1988). Thus, the test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498 (CCPA 1976).

MPEP §2164.01(a) states:

> There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:
>
> (A) The breadth of the claims;
> (B) The nature of the invention;
> (C) The state of the prior art;
> (D) The level of one of ordinary skill;
> (E) The level of predictability in the art;
> (F) The amount of direction provided by the inventor;
> (G) The existence of working examples; and
> (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The claims recite methods of identifying clones comprising a vaccine target or a diagnostic target from microbes or pathogens. Vaccine targets are known to those of skill in the art as candidate polynucleotides or polypeptide antigens expressed from the polynucleotides that have a potential to be useful as a vaccine. *See* Declaration of Dr. Handfield, ¶ 7. Diagnostic targets are known to those of skill in the art as candidate polynucleotides or polypeptide antigens expressed from the polynucleotides that have a potential to be useful as a diagnostic composition. *See* Declaration of Dr. Handfield, ¶ 7. As described in the response of October 26, 2010, many researchers have recognized that the methods of the invention are useful to identify vaccine and diagnostic targets. *See* Declaration of Dr. Handfield, ¶ 5. Additionally, the specification teaches that the claimed methods can be used to identify vaccine and diagnostic targets from any microbes and pathogens. *See* page 11, lines 5-6.

The Office asserts that "the claims encompass any host, any microbe, any pathogen, any antigen, any antibody, etc. Intended use of the final product as a vaccine or a diagnostic target further exacerbates the lack of enablement since the specification does not disclose a single species of vaccine or diagnostic target. Accordingly, the claim scope is unduly broad with respect to encompassed host, microbe, pathogen, antibody, antigen, vaccine, and diagnostic target. " *See* page 8.

Applicants note that the claims are drawn to a method of screening that identifies vaccine targets and diagnostic targets. The vaccine targets and diagnostic targets are therefore identified using the methods and need not be disclosed in the specification. Nevertheless, contrary to the Office's assertion, working Example 5 provides an example of the use of polypeptides identified using the methods of the invention as diagnostic reagents to detect *A. actinomycetemcomitans* antibodies in periodontitis patients.

The term "antigen" does not appear in claims 18 and 19, therefore, it is unclear how this term is allegedly not enabled.

The step of "adsorbing the antibody sample with cells or cellular extracts of the microbe or pathogen that have been grown *in vitro*" can be used and made by one of skill in the art as described in the specification (see page 12, lines 14 through page 13, line 8) and demonstrated in working examples (see Example 1). The Office has not provided any scientific reasoning or explanation to support the assertion the phrase is "unduly broad."

The Office relies upon bald assertions that the claims are "unduly broad" with absolutely no supporting evidence or reasoning to support the assertion. "[I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." *In re Marzocchi*, 439 F.2d 220, 224 (CCPA 1971).

Regarding the state of the prior art and level of predictability in the art, the Office asserts that years of research are necessary to develop potential vaccines and vaccine candidates. The Office concludes that "[w]hile development of vaccines and diagnostics is important, the state of the art requires vast amounts of data including discovery of single or multiple antigens and definitive experiments to ensure that the antigen(s) are sufficiently immunogenic; various

animal studies using various animal models; and phase 0, II, III, and IV trials." The Office cites Sharma and Ramjeet to support their position.

Applicants remind the Office that the claims are directed to methods of screening for vaccine targets and diagnostic targets. Dr. Handfield's declaration states "[t]hose of skill in the art have also recognized that the polynucleotides and the polypeptides expressed from the polynucleotides discovered using IVIAT are important vaccine targets and diagnostic targets, just as described by the specification." *See* ¶ 4. This statement is backed-up with several quotations from peer-reviewed articles that demonstrate that the methods of the invention were indeed actually used by those of ordinary skill in the art. *See* ¶ 5.

Those of ordinary skill in the art have indeed been able to identify diagnostic targets and vaccine targets using only the guidance provided in the specification as filed as demonstrated by Dr. Handfield's declaration.

In fact, Sharma and Ramjeet recognize that the discovery of vaccine targets or vaccine candidates are important in vaccine development. Ramjeet reports "subunit vaccine candidates" at pages 26-29. Sharma reports "target antigens" for vaccine development at pages 581-583. The identification of vaccine targets and diagnostic targets does not require "vast amounts of data including discovery of single or multiple antigens and definitive experiments to ensure that the antigen(s) are sufficiently immunogenic; various animal studies using various animal models; and phase 0, II, III, and IV trials" as alleged by the office and as by demonstrated by Dr. Handfield's Declaration, ¶ 5 and Sharma and Ramjeet.

Regarding the amount of direction provided by the inventor and the existence of working examples the Office asserts that the working examples of the invention do not provide any information regarding vaccine development or use as diagnostic targets. This is incorrect because working Example 5 provides an example of the use of polypeptides identified using the methods of the invention as diagnostics to detect *A. actinomycetemcomitans* antibodies in periodontitis patients.

The Office asserts that the quantity of experimentation needed to make or use the invention based on the content of the disclosure is undue. However, as demonstrated by Dr. Handfield's declaration, those of ordinary skill in the art were able to identify vaccine targets and diagnostic targets using only the methods described in the specification without undue experimentation. Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 1-5, 7, 8, 10, 18 and 19 Under 35 U.S.C. § 102(b)

Claims 1-5, 7, 8, 10, 18, and 19 stand as rejected under 35 U.S.C. § 102(b), as allegedly anticipated by Bickel *et al.* WO98/30910. Applicants respectfully traverse the rejection and request that the arguments presented in the Response of October 26, 2010, be considered along with the additional comments presented herein.

During the Examiner Interview, Examiner Steele asserted that the abstract of Bickel teaches the administration of a cell to a host and therefore teaches "obtaining an antibody sample from one or more hosts infected with the microbe or pathogen" of the claims. Applicants respectfully disagree. The abstract of Bickel states that "[t]he immunodepleted antiserum is raised against a particular cell type of interest or subcellular fraction of a particular cell type of interest, and depleted of antibodies that bind antigens from at least one other cell type or subcellular fraction of at least one other cell type." The Office asserts that this teaches an antibody sample from one or more hosts infected with a microbe or pathogen. Bickel, however, is very clear that the antiserum raised against a particular cell type is "antiserum produced by immunizing a suitable host with **proteins derived** from the cell type of interest." *See* page 5, lines 5-8. Figure 1 of Bickel states that their method includes "immuniz[ing a] host with target proteins." Additionally, page 12, lines 24-28, states that "[p]olyclonal antiserum is prepared against proteins of the target cells according to known methods." No where does Bickel teach or suggest that a **whole, infective** microbe or pathogen would be used to immunize the host. It appears the abstract is differentiating between antiserum that is raised against all proteins of particular cell type of

interest and antiserum that is raised against only a subcellular fraction of proteins of particular cell type of interest.

Furthermore, the claims require "obtaining an antibody sample from one or more hosts infected with the microbe or pathogen." Bickel does not teach or suggest obtaining an antibody sample from an infected host, but from a host immunized with proteins obtained from a particular cell type. The methods of the invention require the use of an antibody sample from a host that has been infected with an infectious pathogen or microbe. An animal model or a surrogate *in vitro* system is not required by the methods of the invention. It is well established that microbial infections are complex, dynamic processes that evolve constantly within the host, and that virulence gene expression is modulated in response to the changing environment encountered at the site of infection. *See* Handfield *et al.* Trends Microbiol. 8:336 (2000) (of record). Therefore, all regulated virulence determinants of a host pathogen, such as a human pathogen cannot be identified *in vitro* or in an animal model of infection because it is technically impossible to determine and mimic all of the complex and changing environmental stimuli that occur at the site of an actual host infection, such as a human infection, and reproduce them in an animal model of infection. Work performed using the methods of Bickel would necessarily miss those critical virulence determinants that are specifically induced in infected hosts, such as infected humans.

Finally, during the Examiner Interview, Examiner Steele appeared to assert that the proteins of Bickel could be considered to be "a pathogen." However, the instant specification defines a microbe or pathogen as any kind of a bacterium, a virus, a parasite, a prion, or a fungus. As such, the proteins used for immunization in Bickel are not pathogens as defined by the instant invention.

The claims are not anticipated by Bickel because Bickel does not teach or suggest all elements of the instant claims. Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 1-5, 7-10, 18, and 19 Under 35 U.S.C. § 102(b)

Claims 1-5, 7-10, 18, and 19 stand as rejected under 35 U.S.C. § 103(a), as allegedly obvious over Bickel *et al.* WO98/30910 and Suk *et al*. Applicants respectfully traverse the rejection and request that the arguments presented in the Response of October 26, 2010, be considered along with the additional comments presented herein.

Suk does not cure the deficiencies of Bickel as described above. Suk requires the use of two types of antibody populations (1) antibodies from animals immunized with killed cultured pathogens and (2) antibodies from infected hosts. Suk does not teach or suggest the use of cells or cellular extracts of the microbe or pathogen that have been grown *in vitro* as required by the instant method.

Bickel and Suk in combination do not teach or suggest the methods of the invention. Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 1-5, 7-10, 18 and 19 Under 35 U.S.C. § 112, first paragraph

Claims 1-5, 7-10, 18 and 19 stand as rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. Applicants respectfully traverse the rejection and request that the arguments presented in the Response of October 26, 2010, be considered along with the additional comments presented herein.

The Office must have a reasonable basis to challenge the adequacy of the written description. The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *In re Wertheim*, 541 F.2d 257, 263 (CCPA 1976).

A determination as to whether one skilled in the art would recognize that the applicant was in possession of the claimed invention as a whole at the time of filing should include the following considerations:

a. Actual reduction to practice;

b. Disclosure of drawings or structural chemical formulas;

c. Sufficient relevant identifying characteristics;

i. Complete structure;

ii. Partial structure;

iii. Physical and/or chemical properties;

iv. Functional characteristics when coupled with a known or disclosed correlation between function and structure;

d. Method of making the claimed invention;

e. Level of skill and knowledge in the art;

f. Predictablitiy in the art.

Written Description Guidelines, Rev. 1, March 25, 2008.

The Applicants have reduced the claimed screening methods to practice in working examples. *See* Examples 1-5. The complete structure and physical and chemical properties of all compositions needed to practice the claimed methods are provided by the specification. For example, the following components are needed to practice the methods of the invention:

(1) an antibody sample from one or more hosts infected with a microbe or pathogen; and

(2) cells or cellular extracts of the microbe or pathogen grown *in vitro*.

One of skill in the art would know how to adsorb an antibody sample with cells or cellular extracts of a microbe or pathogen that have been grown *in vitro*; isolate unadsorbed antibodies; probe an expression library with antibodies; and isolate clones from the expression library. Additionally, the specification provides detailed descriptions of these steps and a working example of these steps.

Methods of making the invention are described by the specification because all of the components needed to practice the claimed methods are described in the specification as are all the techniques needed to practice the inventions as described above. The level of skill and knowledge in the art is high.

The Office's assertions of lack of written description focus heavily on law or rules for determining if **compositions** have adequate written description. For example, the Office cites *Fiddes v. Baird*, 30 U.S.P.Q.2d 1481, 1483 (Bd. Pat. Appl. Int. 1993) for teaching that "claims directed to mammalian FGF's were found unpatentable due to a lack of written description for the broad class

wherein the specification provided only the bovine sequence" and cites *Noelle v. Lederman*, 69 U.S.P.Q.2d 1508, 1514 (Fed. Cir. 2004) for teaching that "there is a lack of written descriptive support for an antibody defined by its binding affinity to an antigen that itself was not adequately described." Applicants are not claiming compositions; rather, they are claiming screening methods where all components and techniques necessary to use the screening methods are described in detail in the specification along with working examples.

The Office relies heavily on *Ariad Pharmaceuticals, Inc. v. Eli Lilly & Co.*, 94 U.S.P.Q.2d 1161 (Fed. Cir. 2010). In *Ariad*, the issue was whether adequate written description existed for genus claims that encompassed the use of all substances that reduce the binding of NF-κB to NF-κB recognition sites. *See* 1164. The specification provided a list of three types of molecules with the potential to reduce NF-κB activity in cells. *See id.* The claims recited methods encompassing a genus of materials achieving a stated useful result, *i.e.*, reducing NF-κB binding to NF-κB recognition sites in response to external influences. *Id.* at 1172. Since the claims recite a genus by its function or result, the specification must recite sufficient materials to accomplish that function. *See id.* at 1173. The court found that the specification did not adequately describe molecules that could reduce NF-κB activity in cells because specific examples of the three types of molecules prophesized to be capable of reducing NF-κB activity were not disclosed or were not adequately described as being able to be used to reduce NF-κB activity. *See id.* at 1176.

The instant claims are different from those in *Ariad*. That is, they recite a screening method where all compositions and techniques necessary to perform the method are adequately described in the specification.

The Office asserts that:

> A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a

written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species).

In *Fujikawa*, the issue was whether a certain **sub-genus of compounds** had written description in the specification, which disclosed a laundry list of every possible moiety at every possible position. *See Fujikawa* at 1904. The specific sub-genus of compounds were found not to have adequate written description because "simply describing a large genus of compounds is not sufficient to satisfy the written description requirement as to a **particular species or sub-genus**." *Id.* at 1905 (emphasis added). The claims of the instant invention are not drawn to a particular species or sub-species of compounds.

Furthermore, The Office asserts that "regardless whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods." This would be relevant case law if the Applicants were claiming the clones or polynucleotides discovered by the screening methods of the invention or if the Applicants were claiming uses of specific clones polynucleotides discovered by the screening methods of the invention. The Applicants, however, are claiming screening methods, not the actual clones or polynucleotides that are discovered by use of the screening methods.

The claims have written description without the description of each and every clone or polynucleotide that could be discovered using the screening methods of the invention. In holding otherwise, the Office would negate the patentability of all screening methods.

The Office asserts that "Applicants have not adequately described the genus of reagents necessary to perform the presently claimed method (e.g., antibodies that bind only antigens expressed *in vivo*, etc. for any microbe or pathogen). Applicants note that "antibodies that bind only antigens expressed *in vivo*" are not reagents necessary to perform the presently claimed method, but rather a characteristic of the product obtained from using the methods of the

invention. Applicants respectfully request clarification as to what reagents are referred by the "etc."

The Written Description Guidelines, Revision 1, of March 25, 2008, present an example of a written description analysis of claims to methods of identifying compounds:

> **Example 17:** Methods Using Compounds Claimed by Functional Limitations, Methods of Identifying Compounds, and Compounds So Identified
>
> **Specification:**
>
> The specification discloses the nucleotide sequences of the coding and promoter regions of two genes that encode the human enzymes POPKIN-1 and POPKIN-2, and a comparison of those sequences. The specification characterizes the enzymatic activity of POPKIN-1 and POPKIN-2 as the same activity. The specification also describes how to make cells that express either POPKIN-1 or POPKIN-2, but not both. The specification describes assays using these cells to screen for compounds which selectively inhibit the expression or activity of POPKIN-2 but not POPKIN-1. "Selective inhibition" is defined as the ability to inhibit POPKIN-2 activity but not POPKIN-1 activity. The specification describes methods of treating specified diseases characterized by aberrant POPKIN-2 activity, using compounds to be identified in screening assays to selectively inhibit POPKIN-2. There are no known compounds that selectively inhibit POPKIN-2 and none are disclosed in the specification.
>
> **Claims:**
>
> Claim 1: A method for selectively inhibiting POPKIN-2 activity in a patient, comprising administering a compound that selectively inhibits activity of the POPKIN-2 enzyme.
>
> Claim 2: A method for identifying a compound that selectively inhibits POPKIN-2 activity comprising
>
> (a) contacting a test compound with a cell expressing POPKIN-2 but not POPKIN-1 and measuring POPKIN-2 activity,
>
> (b) comparing the measured activity from step a to the activity of POPKIN-2 in a non-contacted control cell, and if the measured activity of step a is less than the measured activity of POPKIN-2 in the control cell then,
>
> (c) contacting the compound with a cell expressing POPKIN-1, but not POPKIN-2 and measuring POPKIN-1 activity, and
>
> (d) comparing the measured POPKIN-1 activity from step c to the activity of POPKIN-1 in a non-contacted control cell, wherein,

if the measured POPKIN-1 activity of contacted and control cells is the same, a compound that selectively inhibits POPKIN-2 is identified.
Claim 3: A compound identified by the method of claim 2.

. . .

Claim 2

The claim is drawn to a screening assay for identifying compounds that selectively inhibit the activity of POPKIN-2, but not POPKIN-1. The claim does not limit the compounds that may be used in the assay.

The specification does not describe the complete structure, partial structures, physical properties, or chemical properties of a compound that selectively inhibits POPKIN-2 activity, nor does the specification describe any correlation between the sequences of POPKIN-1 and POPKIN-2 and the structure of any compounds that would selectively inhibit POPKIN-2 activity. The specification does describe the claimed method of screening compounds for selective inhibition of POPKIN-2 activity, reciting the instant steps for identifying a compound with the desired activity.

The level of skill and knowledge in the art is such that one would be able to follow the detailed steps of the claimed method. The practice of the method requires no knowledge of the structures and properties of a compound that would predictably result in the desired activity; rather the claimed invention is the screening process, not the compounds screened or the compounds identified via the claimed process. Thus, one of ordinary skill in the art would conclude that the applicant would have been in possession of the claimed method for identifying compounds that selectively inhibit POPKIN-2 activity at the time of filing.

Conclusion:

The specification satisfies the written description requirement of 35 U.S.C. 112, first paragraph, with respect to claim 2.

Like claim 2 of Example 17 of the Written Description Guidelines, the instant claims are drawn to a screening assay for identifying polynucleotides of a microbe or pathogen that are expressed only *in vivo*. The claims do not limit what microbe or pathogen can be used in the screening assay. The specification does not describe polynucleotides of a microbe or pathogen that are expressed only *in vivo* other than *Actinobacillus actinomycetemcomitans* polynucleotides.

The level of skill in the art is such that one would be able to follow the detailed steps of the claimed method. The practice of the method requires no knowledge of the structures and properties of the polynucleotides that are expressed only *in vivo*; rather the invention is a screening process, not the polynucleotides screened or the compounds identified via the claimed process. Thus, one of skill in the art would have been in possession of the claimed method for identifying polynucleotides of microbes or pathogens that are expressed only *in vivo* at the time of filing. Therefore, the specification satisfies the written description requirement. Applicants respectfully request withdrawal of the rejection.

Rejection of Claims 1-5, 7-10, 18 and 19 Under 35 U.S.C. § 112, second paragraph

Claims 1-5, 7-10, 18 and 19 stand as rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Applicants respectfully traverse the rejection and request that the arguments presented in the Response of October 26, 2010, be considered along with the additional comments presented herein.

The Office asserts that:

> After method step d, the statements "wherein a polynucleotide . . . is isolated" (claim 1), "wherein a vaccine target . . . is isolated" (claim 18), and "wherein a diagnostic target . . . is isolated" (claim 19) are present. However, it is not clear if this is a separate method step.

The claims have been amended to recite methods of isolating clones comprising a vaccine target, a polynucleotide, or a diagnostic target. One of skill in the art would understand that the when the clones are isolated from the expression library to which the unadsorbed antibodies bind, that the polynucleotide/vaccine target/diagnostic target is isolated within the clone. Therefore, one of skill in the art would understand what is claimed when the claim is read in light of the specification.

The Office also asserts that: "method step a has [a] statement that appear[s] to be 'product-by-process' limitation regarding the reagents utilized (i.e. cell or cellular extracts of the microbe or pathogen 'that have been grown *in vitro*')". This issue was discussed in the response filed on October 26, 2010.

The claims are definite and Applicants respectfully request withdrawal of the rejection.

Provisional Rejection of Claims 1-5, 7-10, 18 and 19 on the Ground of Nonstatutory Obviousness-Type Double Patenting

Claims 1-5, 7-10, 18 and 19 stand as provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims 1-16 of copending application 12/327,056.

Applicants note that this rejection is not ripe because neither of the applications has been allowed. The Office, however, states that the claims of the instant invention and those in U.S. Ser. No. 12/327,056 are not patently distinct because "both the presently claimed inventions the inventions as claimed in U.S. applicant 12/327,056 are drawn to methods of isolating a polynucleotide from a microbe utilizing antibodies and antigens." Applicants note that the method steps of the claims in the two applications are different and are indeed patently distinct.

Applicants respectfully request withdrawal of the rejection.

Respectfully submitted,

Dated: December 1, 2010 By: /Lisa M.W. Hillman/
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